Guidelines for the Diagnosis and Management of Acute Chest Syndrome in Adults with Sickle Cell Disease

Acute chest syndrome (ACS) is a serious and potentially life threatening complication of sickle cell disease. Clinical progression can be rapid, leading to respiratory failure. Vigilance throughout admission for the development of this complication is essential. Early recognition and prompt intervention usually results in clinical improvement. Conversely, delay in recognition and treatment can lead to adverse outcomes. ACS occurs in all genotypes of sickle cell disease (SCD).

Clinical features

Hypoxia, tachypnoea, shortness of breath and tachycardia are the cardinal features of chest syndrome. Some of the other features outlined below may also be present.

- Chest pain (sometimes pleuritic)
- Cough (may be productive)
- Shortness of breath
- Hypoxia- oxygen saturation <94% or more than 3% below baseline
- Fever
- Tachypnoea
- Wheeze
- Tachycardia
- Fall in haemoglobin

Chest signs include crepitations, bronchial breath sounds, reduced air entry and dullness to percussion. Rhonchi may be heard. In the early stages, chest examination may be normal.

Diagnosing ACS:

- ACS is largely a clinical diagnosis, particularly in the initial stages.

- Acute chest syndrome can be defined as the presence of a new pulmonary infiltrate on chest X-ray in combination with respiratory symptoms and or fever in a patient with sickle cell disease. It is sometimes referred to as chest crisis. The chest X-ray may however be normal initially, even in the presence of significant respiratory distress.

  If there is strong clinical suspicion of ACS, urgent management should not be delayed pending a chest X-ray. Close monitoring should be instituted together with supportive measures and urgent transfusion considered, particularly in the presence of severe hypoxia.

- Vigilance in patients admitted with vaso-occlusive crisis and in the postoperative period is paramount. Patients may have characteristic clinical features on initial presentation,however, 50% of patients with acute chest syndrome present initially with a painful crisis and then go on to develop ACS. There is also an increased risk of developing ACS post operatively particularly following abdominal surgery.

- Adequate monitoring on the ward is essential to prevent morbidity and mortality from this condition. At least four hourly pulse oximetry and respiratory rate, as well as daily chest examination are essential. Any patient with oxygen saturation < 94% or a fall 3% or more from baseline needs to be reviewed by medical staff immediately and appropriate action taken. A chest X-ray is required in any patient with hypoxia, chest pain, respiratory symptoms or

fever but must not delay the institution of urgent clinical management if the patient is very unwell or has rapidly progressive respiratory deterioration.

Aetiology

The major causes of the acute chest syndrome are infection, fat embolism from infarcted bone marrow and intravascular pulmonary sequestration of sickle cells, leading to lung injury and infarction. Bacterial pathogens and viruses are implicated.

Differential diagnosis of hypoxia in sickle cell disease

1. Chest infection
   Clinically ACS may be indistinguishable from a purely infective episode. If in doubt, treat for both. All patients with ACS should receive intravenous antibiotics as part of their management.

2. Pulmonary embolism
   Typically presents with pleuritic chest pain, hypoxia and a normal chest X ray. D- dimers are usually not helpful in SCD, as they tend to be elevated. On clinical suspicion, a CT pulmonary angiogram should be performed and treatment dose heparin initiated pending CT report.

3. Over-narcosis (Opiate toxicity)

4. Underventilation due to pain

5. Fluid overload

Investigations

- Urgent Chest X-ray
  This should be performed on clinical suspicion of ACS. Findings range from an area of focal consolidation to extensive bilateral multi-lobe opacities. Lower lobe involvement occurs most commonly. Pleural effusions may be present. Be aware that radiology changes may lag behind clinical findings and the diagnosis should be considered even in the absence of radiological changes.
- Arterial blood gases on room air
- Full blood count, reticulocyte count, serum biochemistry, LDH, clotting screen, HbS%, CRP
- Group and antibody screen
- Cross match blood as necessary
- Microbiology
  - Blood cultures in all cases
  - Sputum m,c&s
  - Sputum viral DNA PCR/culture
  - Atypical serology *(repeat after 3 weeks)*
  - Urine for legionella and pneumococcal antigen
  - Nasopharyngeal aspirate- consider if coryzal symptoms/ flu season

Management

- Involve Consultant Haematologist/Haematology SpR once ACS suspected

- Liaise with high dependency /intensive care unit as required. Early warning track and trigger systems should be in place. Some patients will require ventilatory support.

- <u>Monitoring</u>
  Vital signs including sedation scores will need to be assessed more frequently than done routinely. Continuous pulse oximetry is desirable. Clinical review at least four hourly.

- Transfusion
  In ACS, consider blood transfusion early. The degree of hypoxia and respiratory compromise partly governs the need for and mode of blood transfusion. Prompt transfusion often results in a fairly rapid response as timing rather than target haemoglobin S% is important at this stage.
  Simple top up transfusion may suffice early in the course of ACS and may also be used if Hb <6g/dl,aiming for a post transfusion haemoglobin no greater than 10g/dl.
  When indicated, exchange transfusion should be carried out, manually if automated red cell exchange is not readily available.

  Exchange transfusion is indicated in the following circumstances

  - PaO2 < 8kPa on air
  - Deteriorating patient
  - Respiratory distress
  - Multi-lobe infiltrates
  - When a top up transfusion is likely to result in a detrimental increase in blood viscosity
  - In the presence of other significant acute organ dysfunction
  - Progression or limited improvement following top up transfusion.

  Exchange blood transfusion in this setting, should preferably be carried out on a monitored unit such as HDU. Blood should be sickle negative, preferably less than 7 days old and also matched for Rh D, C, E, c, e as well as Kell antigens.

- Oxygen therapy
  Aim to keep oxygen saturations >96%.

- Chest physiotherapy should be undertaken.
  Incentive spirometry has been shown to be beneficial in children.

- Antimicrobials
  Broad-spectrum antibiotics including cover for atypical organisms. The choice is guided by local policy e.g. intravenous augmentin/cefuroxime/ceftriaxone and oral clarithromycin/doxycycline. Close liaison with microbiology is helpful. Specific guidance is required for pandemic flu.

- Hydration
  Oral or intravenous fluids with care taken to avoid fluid overload. A fluid balance chart should be maintained.

- Pain control
  Adequate analgesia in patients with rib, thoracic or abdominal pain is recommended so as to prevent splinting of the diaphragm and the consequent vicious cycle of hypoventilation, atelectasis, hypoxia and sickling that can occur. Due consideration should be given to the optimal safe use of opiates. Monitoring to prevent over narcosis and hypoventilation should be in place. Non-steroidal anti-inflammatory drugs are useful.

- Thromboprophylaxis
  Low molecular weight heparin such as 40mg Clexane subcutaneously is recommended in the absence of any contraindications.

- Nebulised bronchodilators
  Beneficial particularly in the presence of reactive airway signs or if there is history of asthma.

Prevention

- During crisis
  Patients who present in sickle crisis with chest, sternal, rib or back pain, and post abdominal surgery should commence incentive spirometry or chest physiotherapy.

- Secondary prevention
  Hydroxycarbamide has been shown to reduce the incidence of ACS and should be considered in any patient who has 1 or more episode of acute chest syndrome.

- Blood transfusion
  This should be considered prior to surgery in patients deemed to be particularly at risk taking into account past history of ACS, severity of phenotype and or type of surgery planned.

- Other useful measures
  - Optimize vaccination status
  - Penicillin prophylaxis (erythromycin if allergic to penicillin)
  - Smoking cessation
  - Consider echocardiogram and pulmonary function tests– at least 4 weeks following acute episode

References:

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2. Gladwin MT, Vichinsky E. Pulmonary complications of Sickle Cell Disease. N Engl J Med 2008;359(21):2254-65

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